

**REMARKS**

Claims 1-4, 6-17 and 19-34 are pending. By virtue of this response, claims 1-4, 15-17, 19, 32-34 are amended. Claims 16, 17, and 19-31 are withdrawn. Therefore, claims 1-4, 6-15 and 32-34 are presently under examination. Amendment of certain claims is not to be construed as a dedication to the public of any of the subject matter of the claims as previously presented. No new matter is added. Support for the claim amendments may be found throughout the specification including, without limitation, page 13, lines 24-29, page 21, lines 20-22, and page 22, lines 20-24.

**I. Claim Rejections Under 35 USC §112, Second Paragraph**

Claims 3 and 32-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants have amended claim 3 to more closely match the claim format requirements of 37 CFR § 1.75(e). Applicants therefore respectfully request that the Examiner withdraw the rejections of claims 3 and 32-34.

**II. Claim Rejections Under 35 USC §102 - Packer**

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Packer *et al.* (Glycoconjugate Journal vol. 15, pp.737-747, 1998).

Applicants respectfully traverse the rejection and its supporting remarks. Packer *et al.* clearly fails to anticipate the claimed invention, as it does not provide a teaching of analysis of samples that comprise “capsular saccharides conjugated to carrier protein and unconjugated capsular saccharides.” Conjugation to a carrier protein was previously found in claim 5, which the Examiner did not include in the anticipation rejection, thus acknowledging that Packer *et al.* fails to disclose this element.

Applicants therefore respectfully request that the Examiner withdraw the rejections of claims 1-3.

### **III. Claim Rejections Under 35 USC §103 – Bardotti in view of Hennion**

Claims 1-9 and 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bardotti et al. (Vaccine 18: 1982-1993, 3 April 2000) in view of Hennion, MC. (Journal of Chromatography A, vol. 856, pp. 3-54 September 24, 1999).

Applicants respectfully traverse the rejection and its supporting remarks. As discussed on page 2, lines 7-16 and elsewhere in the specification, the inventors have found a method for quickly and reproducibly separating conjugated capsular saccharides from unconjugated capsular saccharides, through the use of solid phase extraction (SPE). As explained in the “Background of the Invention” section of the disclosure, prior to the present disclosure, various methods for separating unconjugated capsular saccharides from conjugated capsular saccharides were available (e.g. ultrafiltration, hydrophobic chromatography, and selective precipitation), but these techniques were slow, poorly reproducible, and frequently depended on the nature of the capsular saccharide (page 1, lines 34-35 through page 2, lines 1-2). By contrast, the SPE-based method of the present disclosure for separating conjugated capsular saccharides from unconjugated capsular saccharides is fast, reproducible, and importantly, as compared with previously known techniques, does not depend on the nature of the capsular saccharide (page 2, lines 9-11). Thus, the technique is particularly useful for analyzing compositions that may contain multiple different types of capsular saccharide, such as combination vaccines containing multiple bacterial saccharide antigens.

The Examiner fails to provide an adequate teaching, suggestion or motivation to arrive at the claimed invention.

As indicated in MPEP Section 2141(II)(A)-(C), assessing obviousness is a three step procedure initially set out by the Supreme Court in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966):

- (A) Determine the Scope and Content of the Prior Art
- (B) Ascertain the Differences Between the Claimed Invention and the Prior Art
- (C) Resolve the Level of Ordinary Skill in the Art

Turning to the teachings of the references cited by the Examiner, Bardotti *et al.* teaches the separation of unconjugated saccharide from conjugated saccharide through ultrafiltration (one of the available methods discussed above), but does not teach SPE. Hennion teaches general information regarding SPE, but it does not provide any teaching of separating unconjugated capsular saccharide from conjugated capsular saccharide by SPE, or the SPE can be used in a manner that allows such separation without being dependent upon the nature of the capsular saccharide. Thus, an important difference between the art cited by the Examiner and the present claims is that neither of the cited references teach that SPE can advantageously be used for the separation of unconjugated saccharide from conjugated saccharide.

To address this deficiency, the Examiner states that it “would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to use a solid phase extraction device in the method of Bardotti *et al.* to obtain the instant invention. One of ordinary skill in the art would have been motivated by the teachings of Hennion to use a solid phase extraction device (SPE) because of its popularity in sample preparation method and reduction in usage of organic solvents in the laboratories which has encouraged the requirement for solvent free procedures and growth of SPE.” Applicants respectfully assert that neither of these reasons are insufficient to establish the obviousness of the pending claims.

According to the MPEP, “[t]he key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious” (MPEP 2142). As indicated above, the Examiner stated that one of ordinary skill would have been motivated to use the SPE teachings of Hennion with the method of Bardotti *et al.* because of SPE’s “popularity.” The fact that one reference teaches a “popular” technique does not, in and of itself, establish the obviousness of combining that reference with another reference to arrive at a claimed

invention. Instead, the Examiner must articulate a reason to combine the references to arrive at a claimed invention. In this case, the Examiner's citation to "popularity" fails to provide an adequate teaching, suggestion, or motivation that would have led one of ordinary skill in the art to combine Bardotti *et al.* and Hennion to arrive at the claimed invention. Scientists are not lemmings that follow other scientists simply to follow a trend. A scientist would look at the reason why a technique or technology is "popular" to understand whether the reason benefits their particular project or need.

The only such underlying reason cited by the Examiner is reduction of "usage of organic solvents in the laboratories." This similarly fails to provide an adequate teaching, suggestion, or motivation that would have led one of ordinary skill in the art to combine Bardotti *et al.* and Hennion to arrive at the claimed invention. A scientist of ordinary skill would have no reason to modify Bardotti *et al.* in view of Hennion to reduce "usage of organic solvents in the laboratories." In Bardotti *et al.*, the method for separating conjugated and unconjugated saccharides uses aqueous, not organic, solvents. In Bardotti *et al.*, unconjugated saccharides are separated from conjugated saccharides through ultrafiltration, using 0.9% NaCl solution (Bardotti *et al.*, page 1983, left column). In contrast, Hennion frequently provides for the use of organic solvents (e.g. page 13, left column "octanol"; page 15, right column "acetonitrile", "methanol"; etc.). Thus, modifying Bardotti *et al.* in view of Hennion would actually increase, not decrease, the use of organic solvents. For at least this reason, a person of skill in the art seeking to reduce "usage of organic solvents in the laboratories" would have no motivation whatsoever to modify Bardotti *et al.* in view of Hennion.

Additionally, Applicants respectfully note that Hennion does not provide a teaching of a method for separating unconjugated saccharides from conjugated saccharides, or teach a separation method that does not depend on the nature of the saccharide. A person of skill in the art seeking to improve the method of Bardotti *et al.* would have no reason to modify Bardotti *et al.* in view of Hennion, because Hennion provides no discernable benefit for the separation of unconjugated saccharides from conjugated saccharides over the method Bardotti *et al.*

Accordingly, Applicants respectfully assert that for at least these reasons, it would not have been obvious for one having skill in the art to combine Bardotti *et al.* and Hennion to arrive at the claimed invention.

Applicants therefore respectfully request that Examiner withdraw the rejections of claims 1-9 and 32-34.

#### **IV. Claim Rejections Under 35 USC §103 – Lei in view of Hennion**

Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lei *et al.* (Dev. Biol (Basel) vol. 103, pp. 259-264, 2000) in view of Hennion, MC. (Journal of Chromatography A, vol. 856, pp. 3-54, September 24, 1999).

Applicants respectfully traverse the rejection and its supporting remarks.

The Examiner fails to provide an adequate teaching, suggestion or motivation to arrive at the claimed invention.

As discussed above, assessing obviousness is a three step procedure as provided in MPEP Section 2141(II)(A)-(C). Turning to the teachings of the references cited by the Examiner, Lei *et al.* teaches the separation of unconjugated saccharide from conjugated saccharide by selective precipitation, but does not teach SPE. Hennion teaches general information regarding SPE, but it does not provide any teaching of separating unconjugated capsular saccharide from conjugated capsular saccharide by SPE, or the SPE can be used in a manner that allows such separation without being dependent upon the nature of the capsular saccharide. Thus, an important difference between the art cited by the Examiner and the present claims is that neither of the cited references teach that SPE can advantageously be used for the separation of unconjugated saccharide from conjugated saccharide.

To address this deficiency, the Examiner states that it “would have been prima facie obvious to one of ordinary skill in the art at the time of invention to use a solid phase extraction device in the method of Lei *et al.* to obtain the instant invention. One of ordinary skill in the art

would have been motivated by the teachings of Hennion to use a solid phase extraction device (SPE) because of its popularity in sample preparation method and reduction in usage of organic solvents in the laboratories which has encouraged the requirement for solvent free procedures and growth of SPE.” Applicants respectfully assert that these reasons are insufficient to establish the obviousness of the pending claims for the same reasons discussed above regarding Bardotti *et al.*

In Lei *et al.* as in Bardotti *et al.*, the method for separating conjugated and unconjugated saccharides uses aqueous, not organic, solvents. In Lei *et al.*, unconjugated saccharides are separated from conjugated saccharides by the addition of deoxycholic acid (DOC) to the saccharide sample. Lei *et al.* states that the DOC solution was “prepared first by either dissolving DOC in pH $\geq$ 12 solution or by directly dissolving DOC sodium in salt water” (Lei *et al.*, page 260, middle). In contrast, Hennion frequently provides for the use of organic solvents (e.g. page 13, left column “octanol”; page 15, right column “acetonitrile”, “methanol”; etc.). Thus, modifying Lei *et al.* in view of Hennion would actually increase, not decrease, the use of organic solvents. For at least this reason, a person of skill in the art seeking to reduce “usage of organic solvents in the laboratories” would have no motivation whatsoever to modify Lei *et al.* in view of Hennion.

Additionally, as noted above, Applicants respectfully note that Hennion does not provide a teaching of a method for separating unconjugated saccharides from conjugated saccharides, or teach a separation method that does not depend on the nature of the saccharide. A person of skill in the art seeking to improve the method of Lei *et al.* would have no reason to modify Lei *et al.* in view of Hennion, because Hennion provides no discernable benefit for the separation of unconjugated saccharides from conjugated saccharides over the method Lei *et al.*

For at least these reasons, the Examiner has failed to establish the obviousness of the pending claims over Lei *et al.* in view of Hennion.

Applicants therefore respectfully request that Examiner withdraw the rejections of claims 1-15.

**CONCLUSION**

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing **Docket No. 223002118900**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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